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How dietary copper affects ruminants

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How dietary copper affects ruminants

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Introduction

Copper is an essential nutrient for the well-being of all animals. In ruminants, copper deficiency may be caused either by inadequate dietary copper (a primary deficiency) or by reduced availability of ingested copper for absorption and utilization (a secondary or "conditioned" deficiency). Excess dietary copper, on the other hand, may accumulate in the liver resulting in copper toxicity. Sheep are more susceptible to copper toxicity than cattle. In both copper deficiency and toxicity cases, farmers can suffer severe financial losses as a result of mortality and lower productivity. However, health and production problems related to copper deficiency are more frequent and economically more important than are the problems associated with copper toxicity.

Primary copper deficiency is caused by a naturally low concentration of copper in the feedstuff and is relatively rare. On the other hand, **conditioned copper deficiency** occurs widespread across Canada and internationally. This latter problem is brought about by various interactions of dietary copper with other substances in the digestive tract, mainly in the rumen. As a result, significant proportions of dietary copper become biologically unavailable, creating shortage in the supply of available dietary copper that is needed for the animal to function normally.

Copper toxicity problems are created when excessive amounts of dietary copper are ingested within a short (**acute toxicity**) or relatively longer (**chronic toxicity**) period. Although chronic copper toxicity is not common in cattle, outbreaks in sheep have been reported in many countries, including Canada. Such outbreaks in sheep are virtually unpredictable and economically devastating to affected producers.

Biological availability of copper

The presence of copper in animal tissue was recognized as early as 1833, but its role as an essential dietary component for ruminants was not conclusively proven until 1931. Since then, copper deficiency has been linked to several health and production problems in ruminants and other animals. It has also been recognized that copper provided in the diet must be in a form that can be metabolized effectively by the animal to meet its needs; on the other hand, toxic accumulation must be prevented. Many factors affect the biological availability of dietary copper for absorption and utilization.

Physiological factors

Age Although preruminant lambs use 47–71% of dietary copper and are considered as efficient as monogastric animals in their absorption of copper, the use decreases to 1–4% by the time sheep reach maturity. This decrease is associated mainly with the development of a fully functional rumen and its resident bacterial and protozoal populations. In the calf, age-related changes in copper metabolism are completed within the first month of life.

Tissue reserves Copper absorption from the intestinal tract is higher in copper-depleted than in copper-adequate animals.

Breed Some sheep breeds are more efficient in absorbing dietary copper than other breeds. In general, sheep bred for wool production, such as Merino, are more susceptible to copper deficiency than are meat breeds. Genetic differences were also demonstrated in cattle. Individuals within the same animal breed or flock also differ in their susceptibility to copper deficiency.

Dietary factors

Chemical forms of copper The form in which copper exists naturally in feeds greatly influences its biological availability. Changes in the chemical form of copper occur during both the maturation of plants and the curing or drying of herbage. When fed to ruminants, copper carbonate and the water-soluble copper sulfate, nitrate, and chloride supplements are absorbed to a greater extent than is copper oxide. Metallic copper is poorly absorbed.

Mineral interactions The elements that markedly affect copper absorption and metabolism in ruminants are calcium, iron, sulfur, zinc, cadmium, and molybdenum. The most serious interactions are those between copper and sulfur and between copper, sulfur, and molybdenum; these interactions result in the formation of insoluble and biologically unavailable copper sulfide or cupric thiomolybdates, respectively. Such compounds are not absorbed from the intestinal tract and are excreted in the feces without being used. If the concentration of dietary sulfur is low, molybdenum has no effect on the biological availability of copper. However, high dietary sulfur, including the organic sulfur released from dietary proteins during ruminal digestion, may react with copper directly and make it unavailable for absorption. For this reason, the copper–sulfur interaction is the most common cause of conditioned copper deficiency in ruminants. However, when the dietary concentrations of both molybdenum and sulfur are high, thiomolybdates are formed in the rumen. A part of these thiomolybdates reacts with copper in the rumen and forms unabsorbable cupric thiomolybdates. The other part of the thiomolybdates is rapidly absorbed and reacts with copper in the blood

and tissues and, in this way, depletes the body of already absorbed copper by the route of urinary excretion. The manifestation of copper deficiency due to the complex interaction between molybdenum, sulfur and copper is very rapid because both the reduction in the dietary copper absorption and the elimination of copper from the body take place at the same time.

Protein Ruminal degradability of dietary protein is a major factor affecting the biological availability of dietary copper. For instance, more copper is required when the animals are on pasture than when dry forage or concentrates are fed. This need is related to higher solubility and, therefore, to higher ruminal degradability of protein in fresh than in dry feed. Higher protein degradability, in turn, contributes to higher ruminal concentration of soluble sulfur and to copper–sulfur interaction.

Copper deficiency

A primary or conditioned copper deficiency is associated with a wide variety of disorders including:

- anemia
- severe diarrhea
- change of hair or wool color
- neonatal ataxia
- infertility
- heart failure
- fragile long bones
- depressed growth.

Not all these signs necessarily occur in every copper-deficient animal. Some signs of copper deficiency may be caused by a single factor, others by a combination. Also, some signs are specific to individual animal species, while others are common to all ruminants. Observations suggest that copper deficiency may affect immunity and decrease resistance to infection.

Symptoms

Anemia Reduced hemoglobin is a general clinical sign of copper deficiency in all ruminants. Copper deficiency restricts the mobilization of iron from tissues, mainly the liver, and thus plays a critical role in the synthesis of hemoglobin.

Diarrhea In cattle, diarrhea is the basic symptom on which the diagnosis of copper deficiency relies. A diarrhea that is cured by a copper treatment has been observed in cattle in numerous regions

throughout the world. It has, however, not been a common manifestation of copper deficiency in most species; the clinical signs of the severe diarrhea differ in sheep and cattle. The diarrhea is more prevalent when excess molybdenum is a major cause of the copper deficiency, which is especially true when its onset is very rapid and quite severe; low dietary copper does not cause this type of diarrhea. Goats were observed to develop scouring when maintained on the same pasture that induces scouring in cattle.

Hair or wool color and appearance The loss of pigment in hair or wool is the most characteristic manifestation of copper deficiency in ruminants. The pigmentation process is so susceptible to changes in the copper status that following a copper-deficient condition, alternating pigmented and unpigmented bands in wool are produced in sheep by adding or withholding copper supplement from the diet. The depigmentation of wool is commonly associated with lower wool production. The wool usually lacks crimp; has reduced tensile strength, abnormal elastic properties, and a "steely" texture; and is, as a result, less valuable.

In copper-deficient cattle, hair color changes depend on the original hair color; white hair may turn a dirty yellow, whereas black hair may become reddish brown. The loss of pigment can also occur around the eyes where it is known as **spectacles** (Fig. 1).

Neonatal ataxia This disease has been observed in sheep, goats, and deer, but not in calves. It is a disorder in the central nervous system caused by copper deficiency and is known throughout the world under a variety of names, most commonly as **swayback** because of the unsteady gait and stance. The incoordination is associated with the lack of myelination in the spinal cord, neuronal damage, and cerebral cavitation. General disorders of the nervous system are the major symptoms in sheep and goats on which the diagnosis of copper deficiency relies.

In sheep and goats, the disease takes two forms:

(1) the common acute form in which the animals are affected at birth (Fig. 2); and

(2) a delayed form that may develop within 3 months (Fig. 3) or in some cases much later (chronic cases). In both forms the signs are essentially those of a spastic paralysis, particularly of the hind limbs with different degrees of severity. All affected animals show incoordination of movements or are unable to stand or walk. In some cases of neonatal ataxia, the animals may become anemic; some become blind.

Fig. 1 Copper-deficient calf with gray hair around the eyes (*top*) and normal calf (*bottom*).

Fig. 2 Day-old twins born with acute form of swayback (congenital ataxia) caused by chronic copper deficiency.

Fig. 3 Two-month old goat with delayed form of ataxia caused by chronic copper deficiency.

Infertility In cattle grazing on copper-deficient pastures, low fertility associated with delayed or depressed estrus and decreased conception rate occurs in many areas. Copper deficiency in cows is also responsible for such effects as calving difficulties, retained placenta, and calves born with congenital rickets. Infertility has also occurred in copper-deficient ewes; in some cases it was associated with aborted small fetuses.

Heart failure Copper is required for metabolic activity of heart muscle. Cardiac failure (sudden death) known as falling disease sometimes occurs in copper-deficient cattle. Some animals have problems with breathing.

Fragile long bones In copper-deficient animals, bones break easily and sometimes without apparent cause. Lameness may also result from copper deficiency. In cattle, particularly calves, the ends of the leg bones swell or enlarge, especially above the fetlocks. Skeletal lesions can occur in both cattle and sheep deficient in copper.

Depressed growth Marginal (subclinical) copper deficiencies are difficult to recognize. However, they are widespread and are more economically significant than easily recognized cases. Affected animals may be unthrifty; have lower milk production, growth, and fertility; and lack readily recognized signs of copper deficiency.

Assessment

Of a wide range of biochemical techniques available to support the diagnosis of copper deficiency, clinical signs, growth response, and especially analyses of feed and tissues are commonly used. The criterion most widely used for copper deficiency is the concentration of copper in the liver.

Feed Although the copper content of feed provides a poor estimate of the copper status in ruminants, it is useful as a beginning point. Feed analysis indicates if a major nutritional deficiency or excess of copper exists.

Blood The normal level of copper in blood plasma or serum is about 0.5–1.5 μg/mL. Levels consistently below 0.5 μg/mL indicate possible copper deficiency. During severe deficiency, the copper levels are around 0.1–0.3 μg/mL. However, blood copper levels are not considered as a good diagnostic aid for detecting copper deficiency in ruminants.

Coat The threshold value for copper in the dry coat is 8 mg/kg and may be as low as 3 mg/kg in deficient animals.

Liver The liver is the main storage organ for copper and the level therein is a useful indicator of the copper status in the animal. In

healthy ruminants, liver copper values (dry matter) normally range between 100 and 400 mg/kg. Copper values below 25 mg/kg indicate the possibility of copper deficiency, and below 10 mg/kg the deficiency is certain.

Copper requirements

Ruminants have higher copper requirements than other livestock. Because of many interactions that influence the bioavailability of dietary copper in ruminants, general recommendations for copper in the diet of cattle and sheep is difficult; suggested ranges for copper in dry matter are 8–10 mg/kg for cattle and 5–10 mg/kg for sheep. However, when the dietary concentrations of sulfur and molybdenum are low, or protozoal population in the rumen is not present, the dietary concentration of 8 mg/kg and over could produce chronic copper toxicity in sheep. Also, copper deficiency may occur in both cattle and sheep with dietary copper intake of 10–12 mg/kg when the dietary concentrations of molybdenum are high (copper : molybdenum ratio less than 2.8 : 1 in the presence of adequate sulfur), or the animals are fed fresh forages containing highly soluble proteins. It is suggested that when dry matter in the diet contains copper at 10 mg/kg, a molybdenum concentration of 0.5–2.0 g/kg and a sulfur concentration of 0.1–0.4% dietary copper metabolism is normal. A ratio for dietary copper to molybdenum of 2.8–6.0 : 1 is considered ideal.

Prevention and treatment

There are two ways of preventing copper deficiency in ruminants:

1) indirect method: by treating soil or plants,

2) direct method: by treating the animal.

The indirect approach is effective mainly in the case of simple copper deficiency. In the case of conditioned deficiency, the best approach is to treat the animals themselves.

Indirect methods Incorporating copper sulfate powder into the soil, or applying a granula form as a top-dressing, in amounts between 5 and 7 kg/ha may increase the copper concentration in the dry matter of the forage by about 5 mg/kg. Although the benefits from such treatment can last for as long as 20 years, good forage is usually produced only for 2–3 years following the application of copper sulfate.

Foliar application of copper sulfate or copper oxide to grassland produced little or no lasting effect on herbage copper concentration. Spraying must be repeated after each cut.

Direct methods Adding copper salts such as copper sulfate to either the concentrate or complete feed mixture is the best way to supplement copper. This method is ideal when ruminants are penned or kept in a

dry lot because each animal is likely to receive the desired dose in its feed. Under grazing conditions, however, this method is usually economically prohibitive.

Copper can be added to the drinking water at the rate of 2–3 mg/L. However, this method may be less satisfactory than other methods of supplementation.

Copper sulfate can be included in licking stones, in proportion of 0.6–1%. Because animals do not like the stones equally, it is difficult to supply the animals with the exact amount of copper required.

Mineral supplements containing 0.1–0.2% copper sulfate are generally consumed voluntarily by grazing animals in amounts sufficient to maintain adequate and safe copper intakes. This method is often the one of choice for grazing animals because forages are often deficient in a number of minerals. Other methods for grazing animals include dosing or drenching at intervals with copper compounds, or by injecting organic complexes of copper.

Drenching at monthly or longer intervals is satisfactory in copper-deficient areas, except where molybdenum contents in the forage dry matter are sufficiently high (over 5 mg/kg) to induce scouring. Under this condition, the copper supplementation must be regular and more frequent.

Oral dosing of pregnant ewes consists of giving 20 mL of a 25% solution of copper sulfate. Lambs under 4 months of age receive 5 mL and those over 4 months of age 5–10 mL of the solution.

Subcutaneous or intramuscular injection is often the chosen way to administer slowly absorbed forms of copper, such as copper glycinate. Most of the copper dose accumulates directly in the liver and gives protection for as long as 4 months. A single subcutaneous injection of 25 mg of copper glycinate in ewes at mid pregnancy is generally sufficient to prevent ataxia in the newborn lambs. The lambs should be given an injection every 3 months. In cattle, a single subcutaneous injection of 120 mg of copper glycinate should be given every 3 months to pregnant cows, three times yearly to young animals, and twice yearly to mature animals.

A novel approach involves the oral administration of soluble capsules containing cupric oxide needles (fragments of oxidized copper wire), or copper-containing controlled-release glass, which are retained within the stomach. Copper is slowly released from these supplements over an extended period. The amount and frequency of dosing is prescribed by the manufacturers of these supplements.

Copper toxicity

The sudden ingestion of large amounts of copper may produce acute toxicity. In chronic toxicity, the ingestion of quantities of copper slightly higher than the requirement increases copper deposition in tissues, mainly liver and kidney. For a time this deposition is tolerated, but at a particular concentration clinical signs of toxicity appear.

Acute toxicity

Acute copper toxicity is relatively uncommon. It may arise after either a single or a small number of large oral doses of copper, or a parenteral injection of copper preparations used for treatment of copper deficiency.

Acute toxicity is produced by copper concentrations in dietary dry matter of 20–50 mg/kg for lambs, 130 mg/kg for sheep, and 200 mg/kg for adult cattle. The symptoms of the acute oral toxicity are acute gastroenteritis with abdominal pain, diarrhea, and sometimes death. Following the toxic injection of copper preparations, animals may become weak and show yellow discoloration of the mucous membranes or may be found dead. Death usually occurs within 3 days of the injection in sheep, but within up to 12 days in calves.

Chronic toxicity

The occurrence of chronic copper toxicity has long been recognized as a major hazard in the intensive rearing of sheep, but much less in cattle. The ovines are much more sensitive to chronic copper toxicity than are the bovines.

Continued ingestion of copper in excess of requirements leads to accumulation in tissues, especially the liver, for weeks or months (prehemolytic phase). The liver cells can retain large amounts of copper without apparent harm or clinical signs. Beyond certain levels, a liberation of a high proportion of the liver copper into the blood stream can occur, resulting in extensive hemolysis characterized by yellow eyes (icterus) and jaundice (hemolytic phase). Animals with a milder form of the disease may survive, but others die in a few hours. On autopsy, copper toxicity is characterized by black kidneys and fat necrosis (yellow fat) mainly around internal organs. During a severe hemolytic phase the animal usually becomes dull, passes soft feces, loses its appetite, exhibits an excessive thirst, and excretes dark urine. The surviving animals enter a posthemolytic phase during which clinical signs return to normal.

Outbreaks of chronic copper toxicity have occurred in Canada and elsewhere. In most cases the cause of the outbreak remains unknown. More recently, however, there was an outbreak in sheep at the Centre for Food and Animal Research in Ottawa. The flock has been reestablished by hysterectomy to eradicate maedi-visna disease. The new crop of lambs was not reinfected with ruminal protozoa and remained fauna-free. Almost 40% of new lambs died from chronic copper toxicity, which was found to have been caused by the absence of protozoa from the rumen. It was discovered that protozoa may alleviate the toxicity by contributing to ruminal interaction between copper and sulfur, thus decreasing the biological availability of dietary copper by about 30%.

Prevention and treatment

In sheep fed diets high in copper, supplementation with zinc at 175–375 mg/kg may prevent the development of copper toxicity. After a diagnosis of copper toxicity, trace elements in the diet should be adjusted to more appropriate levels or the diet replaced.

Following removal of the source of excess copper, signs of chronic copper toxicity and even death may occur because of continued ruminal availability and high tissue levels of copper. The most-used preventive method in sheep for this purpose is the daily oral administration of sodium sulphate (0.3–1 g) and ammonium molybdate (50–500 mg) for up to 3 weeks. Another method is to administer strong chelators of copper such as penicillamine. This method is very expensive. Also, intravenous injection of 100 mg of ammonium tetrathiomolybdate may prevent hemolytic crises and minimize tissue damage in sheep.

Conclusions

Inadequate dietary copper or reduced biological availability of dietary copper cause the health and production problems associated with copper deficiency. Excessive ingestion of copper causes copper toxicity. Both problems may result in substantial economic losses to cattle or sheep producers. Because the biological availability of dietary copper is affected by many factors, such as dietary concentration of sulfur and molybdenum, the concentration of copper in the diet is useful only as a preliminary indicator, if a major nutritional deficiency or excess of copper exists. Other indicators or their combinations, such as blood, coat, and liver copper concentrations, are more sensitive in assessing the copper status of the animal.

If it is established that the ingestion of copper is below the requirement, or if symptoms of the copper deficiency are apparent, proper methods for prevention and treatment of the copper deficiency should be applied immediately. Such methods could consist of treating the soil with copper sulfate or of treating the animal itself with copper preparations.

When ingestion of copper is excessive, the source of the excess of dietary copper must be removed and a preventive method, such as supplementing the diet with sodium sulfate and ammonium molybdate, should be applied to remove excess copper from the body. Failure to do so could result in clinical toxicity or death of affected animals.

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